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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,356	07/02/2003	Ralph Zahn	26563U	5402
20529	7590	06/18/2007	EXAMINER	
NATH & ASSOCIATES 112 South West Street Alexandria, VA 22314			RIGGS II, LARRY D	
		ART UNIT	PAPER NUMBER	
		1609		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/612,356	ZAHN ET AL.	
	Examiner	Art Unit	
	Larry D. Riggs II	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 07 November 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-29 is/are pending in the application.
 - 4a) Of the above claim(s) 10-29 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-9 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 02 July 2003 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>17 September 2003</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The instant application has been forwarded to examiner Larry D. Riggs II of art unit 1609 upon applicant's election.

Election/Restrictions

Applicant's election with traverse of Group I and species Transmissible Spongiform Encephalopathy (TSE) in the reply filed on November 7, 2006 is acknowledged. The traversal is on the ground(s) that areas of search would apply to all Groups, the examiner has powerful electronic search engines and the Groups being in different classifications does not necessarily make them distinct, thus there would not be a search burden on the examiner. This is not found persuasive because different searches would be required for each Group and result in a search burden on the examiner. For example, Group I is drawn to a folding process with specific steps, Groups II, III and V are drawn to products that can be produced by the Group I process. Examination of the products and their uses requires searches of similar product made by different methods, and therefore involves searches not required for Group I.

The requirement is still deemed proper and is therefore made FINAL.

Claims 10-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 7, 2006.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within **the range of 50 to 150 words**. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract should be on a separate sheet of paper. The "Fig.7" should be excluded from the bottom of the page. The abstract is over 150 words and should be within the range of 50 to 150 words.

The disclosure is objected to because of the following informalities:

Figure 8 contains sequence recitations which are not identified by SEQ ID numbers. The required identifiers may be inserted into the brief description of the figure, or an amended figure may be filed.

Appropriate correction is required.

Claim Objections

Claim 1 is objected to because of the following informalities:

The word "protein" should be spelled accordingly, in line 3. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 7-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "a conversion buffer" in claims 1 and 7-9, is indefinite. The term "a conversion buffer" is not defined by the claim. The term implies a category of things and is not defined in the specification.

The term "a conversion temperature" in claim 1 is indefinite. The term "a conversion temperature" is not defined by the claim, the specification does not provide a definition for this term while various individual temperatures and temperature ranges are provided. This term would not allow one of ordinary skill in the art to determine the metes and bounds of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Martinez-Senac et al., *Eur. J. Biochem.* 1999, 265, 744-753 and Esler et al. *Biochemistry*, 1996, 35, 13914-13921.

The instant claim 1 describes a method for increasing beta-sheet content in amyloid proteins by mixing a conversion buffer, lamellar lipid structures with negative charge and recombinant amyloid proteins at a conversion temperature for a time.

Martinez-Senac et al. teaches the increased beta-sheet formation of amyloid peptide when interacting with negatively charged phospholipids vesicles, (see page 746, left column, fifth paragraph; page 751, left column, second paragraph).

The instant claim 9 is dependent from the method of claim 1 that describes the pH of the conversion buffer below the isoelectric point of the recombinant amyloid protein.

Martinez-Senac et al. teaches buffer pH at 3.0, (see figures 3 and 4). This pH is below the beta amyloid peptide isoelectric point of 5.0, (see page 13919, second column, second paragraph).

Thus, Martinez-Senac et al. and Esler et al. anticipate claims 1 and 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martinez-Senac et al., *Eur. J. Biochem.* 1999, 265, 744-753 in view of Barrow et al., *Science*, 1991, 253, 179-182 and Gursky et al. *Biochimica et Biophysica Acta*, 2000, 1476, 93-102 and Luhrs et al. "Evidence for Oligomerisation of Human Prion Protein upon Association with a Bicellar Systems", Symposium, "Characterization and Diagnosis on Prion Diseases in Animals and Man," Tuebingen, Germany, September 23-25, 1999 and Pan et al. *Proc. Natl. Acad. Sci.* 1993, 90, 10962-10966 and Vold et al., *J. Magn. Res. B*, 1996, 113, 267-271.

The instant claims describe a method for increasing beta-sheet content in amyloid proteins by mixing a conversion buffer, lamellar lipid structures with negative charge and recombinant amyloid proteins at a conversion temperature for a time.

The instant claims 2 and 3 are dependent from the method of claim 1 that describe the production of amyloid aggregates once the lamellar lipid structures are destroyed. Martinez-Senac et al. teaches the increased beta-sheet formation of

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amyloid peptide when interacting with negatively charged phospholipids vesicles, (see page 746, left column, fifth paragraph; page 751, left column, second paragraph).

Martinez-Senac et al. teaches the preparation of amyloid peptide in association with negative charged phospholipids dissolved in water formed fibrils, (see page 747, left column, second paragraph). Martinez-Senac et al. does not teach actively destroying the lamellar lipid structures.

Barrow et al. teaches that once a beta-sheet structure is formed in amyloids, the structure leads to the formation of insoluble amyloid fibrils, (page 253, middle column, first paragraph – right column, second paragraph). Barrow et al. teaches that in aqueous solutions, in the absence of TFE, at either low or high pH the amyloid peptides are 100% beta-sheet, causing an insoluble gel to form (page 253, middle column, first paragraph – right column, second paragraph).

One would be motivated to disperse the micelles surrounding amyloid protein with the advantage of showing the amyloid protein was increasing in beta-sheet secondary structure with the formation of insoluble fibrils that occur when amyloid protein is exposed to water. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Martinez-Senac et al. by putting the vesicles in an environment, such as pure water, that would destroy the micelles surrounding the amyloids to produce the insoluble amyloid fibrils as implied by Martinez-Senac et al. and taught by Barrow et al.

The instant claims 4 and 5 are dependent from the methods of claims 1 and 4 respectively, that describe a temperature that increases once the components of the

solution are mixed. Martinez-Senac et al. teaches the increase of beta-sheet formation in amyloids with negatively charged vesicles, (see above). Martinez-Senac et al. does not teach the increase in beta-sheet formation with increase in temperature.

Gursky et al. provides a method for the temperature-dependent beta-sheet formation in amyloids in water. Gursky et al. teaches the increase of beta-sheet formation with the increase of temperature from 0 to 98°C at a rate of 15 deg/h, (see figure 2, page 98, right column, last paragraph – page 99, right column, first paragraph).

One would be motivated to increase the temperature of the solution of amyloid and vesicles with the benefit of increasing the interaction of the phospholipids and the amyloid peptide and thus increase in beta-sheet formation. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Martinez-Senac et al. by increasing the temperature once all components of the mixture were added as taught by Gursky et al.

The instant claim 6 is dependent from the method of claim 4 that describes a temperature that increases once the components of the solution are mixed, wherein the amyloid protein is involved in Transmissible Spongiform Encephalopathy (TSE).

Martinez-Senac et al. teaches the increase of beta-sheet formation in Alzheimer beta-amyloid peptide, with negatively charged vesicles. Martinez-Senac et al. does not teach utilizing amyloidogenic proteins involved in Transmissible Spongiform Encephalopathy (TSE).

Luhrs et al. teaches the use of amyloid protein involved in Transmissible Spongiform Encephalopathy (TSE), (see introduction) in monitoring beta-sheet

formation in negatively charged vesicles, (see figure 1, 3 and conclusion). Pan et al. teaches the conversion of alpha-helices into beta-sheets in the formation of the scrapie prion proteins. Pan et al. teaches that the conversion of alpha-helices in the prion protein into beta-sheets is likely to be the primary lesion in the illness of Spongiform Encephalopathy, page 10965, second paragraph). Pan et al. teaches similar proteins that undergo the conversion of alpha-helices into beta-sheets are betaA4 peptides involved in Alzheimer disease, (see page 10966, first paragraph).

One would be motivated to utilize other proteins that undergo beta-sheet formation that have the propensity to form insoluble fibrils with the benefit of showing the method was applicable to other amyloid class proteins and their associated diseases. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Martinez-Senac et al. by utilizing a protein associated with Transmissible Spongiform Encephalopathy (TSE).

The instant claims 7 and 8 are dependent from the methods of claims 1 and 7 respectively, that describe the conversion buffer comprising short and long chain phospholipids, from the phosphocholine family, DMPX, DHPC, DMPS or DMPG, in concentrations sufficient to produce negative charged phospholipid vesicles. Martinez-Senac et al. teaches the increased beta-sheet formation of amyloid peptide when interacting with negatively charged phospholipid vesicles, made from DMPC, DMPS, DMPG and other members of the phosphocholine family (see page 745, left column, third paragraph). Martinez-Senac et al. does not teach the preparation of negatively charged vesicles with DMPX or DHPC.

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Vold et al. teaches magnetically oriented phospholipid bilayered micelles for structural studies of polypeptides. Vold et al. teaches the binary mixture of long and short chain phosphatidylcholines such as DMPC and DHPC to be consistent with disk-shaped phospholipid aggregates, (see page 267, left column, first paragraph).

One would be motivated to utilize other phosphocholine family members that allowed for the production of charged phospholipid bilayered micelles for the benefit of exploiting lipids that may be more appropriate for particular biological systems. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Martinez-Senac et al. by utilizing other phosphocholine family members such as DMPX or DHPC.

Conclusion

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry D. Riggs II whose telephone number is 571-270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Larry D. Riggs II


MARY MOSHER
SUPERVISORY PATENT EXAMINER
6-8-07